

**14<sup>th</sup> MEETING OF CELLULAR BIOLOGY BASED THERAPEUTIC DRUG EVALUATION COMMITTEE (CBBTDEC), HELD ON 01.06.2018 IN THE CONFERENCE HALL, ICMR, NEW DELHI**

Ministry of Health & Family Welfare, Govt. of India constituted a Core IND panel of experts namely CBBTDEC vide order no. DCG (I)/Misc/2010/2010 (Pt. Stem Cells)/DFQC dated 01/09/2010. The 14<sup>th</sup> meeting of the CBBTDEC was held on 01.06.2018 at 10:00 A.M. in the conference Hall, ICMR Headquarter, Ansari Nagar, New Delhi under the Chairmanship of Prof. Balram Bhargava, Secretary, Department of Health Research & Director General, ICMR, New Delhi.

The following Expert panel members, ICMR members and CDSCO staff attended the meeting:

**Expert Committee Members:**

1. Prof. Balram Bhargava, The Secretary, Department of Health Research & Director General, ICMR, Ansari Nagar, Post Box No. 4911, New Delhi -110029.
2. Prof. Alok Srivastava, Professor & Head, Dept. of Hematology, CMC, Vellore – 632004, Tamil Nadu.
3. Prof. N. K. Mehra, Dean (Research) and Head Dept. of Transplant Immunology and Immunogenetics, AIIMS, New Delhi.
4. Prof. D. Balasubramanian, Director of Research, LV Prasad Eye Institute, K. Anji Reddy Campus, Road No. 2, Banajara Hills, Hyderabad 500034.
5. Dr. Manjari Tripathi, Professor, Department of Neurology, AIIMS, New Delhi (expert for proposal #6)

**ICMR Members:**

Dr. Vijay Kumar, Head, BMS, ICMR

Dr. Geeta Jotwani, Deputy Director General (Scientist 'F'), ICMR, New Delhi.

**CDSCO Staff:**

Dr. S. Eswara Reddy, Drugs Controller General India

Dr. V. G. Somani, Joint Drugs Controller (India)

Mr. Yogesh Shelar, Asst. Drugs Controller (India)

Mr. Varun Kumar, Drugs Inspector

Mr. C. Hemanth Kumar, Drugs Inspector

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The following proposals were considered and various questions raised by the member panel along with the opinion are as follows:

S.No.	Proposal	Recommendation
Agenda 1	<p><b>Agenda 1</b>  <b>Applicant:</b> M/s. Christian Medical College, Vellore.  <b>F.No.</b>X-11026/52/2018-BD</p> <p><b>Presentation:</b> Application for grant of permission to undertake Phase II clinical trial of Autologous Culture expanded iliac crest chondrocyte transplantation in India.</p>	<p>Firm presented the proposed clinical trial before the committee. After due deliberation, the committee recommended that firm shall submit the preclinical and human trial data for proof of concept for consideration of approval of clinical trial. The committee recommended for approval of protocol on submission of these data.</p>
Agenda 2	<p><b>Agenda 2</b>  <b>Applicant:</b> M/s. Stempeutics Research Private Ltd., Bangalore</p> <p><b>F.No.</b> Stm-CI/05/Stempeutics/17-BD</p> <p><b>Presentation:</b> In continuation with the recommendations of the 13<sup>th</sup> CBBTDEC meeting dated 16.11.2017 the firm has submitted the revised Phase III Clinical Trial protocol in compliance with 13<sup>th</sup> CBBTDEC recommendations for the protocol titled as "A randomized, double blind, multicentric, placebo controlled, phase III study assessing the efficacy and safety of intra-articular administration of Stempeucel® (adult human bone marrow derived, cultured, pooled, allogeneic mesenchymal stromal cells) in patients with osteoarthritis of knee" with Protocol No. SRPL/OA/16 -17/001; version No. 02; dated 23.11.2017.</p>	<p>Firm presented the revised phase III trial protocol and after due deliberation the committee recommended the protocol with the condition that:</p> <ol style="list-style-type: none"> <li>1. Clear wording for use of "Rescue medication" (analgesics) shall be incorporated in the protocol &amp; Patient Information sheet.</li> <li>2. The randomization of study subjects shall be done into the two arms based on Osteoarthritis grade II &amp; III.</li> </ol> <p>The committee recommended for approval of protocol after inclusion of these modifications. After inclusion of these modifications, the protocol may be approved.</p>

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<p>Agenda 3</p>	<p><b>Agenda 3</b>  <b>Applicant:</b> M/s. Reliance Life Sciences Mumbai.  <b>F.No.</b>Stm-CI/03/Reliance/15-BD.</p> <p><b>Presentation:</b>In continuation with the recommendations of the 12<sup>th</sup> CBBTDEC meeting dated 01.09.2017 the firm has submitted the response along with the revised Phase-IIa Clinical trial protocol titled as "A prospective, randomized, open label, double arm, controlled multi-centric, clinical study to evaluate the safety and efficacy of R-HSC-010 in prevention of progression of chronic kidney disease stage-III", RLS/RM/HSC/2012/06, version 03 dated 9 Feb 2018.</p>	<p>The firm presented the amended Phase IIa clinical trial protocol before the committee. After due deliberation, the committee opined that,</p> <ol style="list-style-type: none"> <li>1. Firm has not justified the change of trial design from Phase I/II to Phase IIa. Therefore the committee recommended to maintain this study as a Phase I/II protocol.</li> <li>2. The selection of proposed human dose of 4million cells/kg body weight at 2 dose intervals (day 0 and 4 months) was not adequately explained or justified.</li> <li>3. The selection of route of administration by renal artery over other simpler routes (IV) was not substantiated with any evidence or pre-clinical data. Therefore the committee recommended to add arm of IV administration as well unless there are compelling reasons / evidence for arterial administration.</li> </ol> <p>Therefore, the committee did not recommend the proposed clinical trial protocol and asked to submit a revised proposal with adequate details and explanations for placing before the committee.</p>
<p>Agenda 4</p>	<p><b>Agenda 4</b>  <b>Applicant:</b> M/s. Duraent Biological Ltd., Madhapur, Hyderabad.  <b>F.No.</b>X-11026/80/17-BD</p> <p><b>Presentation:</b> In continuation with the recommendations of the 13<sup>th</sup> CBBTDEC meeting dated 16.11.2017 the firm has submitted the technical write up for grant of permission for import of "Amniotic fluid and Amniotic membrane" under the Drugs and Cosmetics Act and Rules there under.</p>	<p>The proposal was not deliberated in the meeting as firm has requested to hold their proposal for deliberation in next CBBTDEC meeting.</p>

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Agenda 5	<p><b>Agenda 5</b>  <b>Applicant:</b> M/s APAC Biotech Pvt. Ltd. Gurgaon,  <b>F.No.</b> Stm-CI/27/APAC BIOTECH/12-BD</p> <p><b>Presentation:</b> Ethics Committee Approval waiver for the PMS study titled "A Post Marketing PMS protocol entitled "A Post Marketing Surveillance study for evaluating safety of APCEDEN<sup>®</sup>, an autologous dendritic cell immunotherapy."</p>	<p>The firm presented the proposal of Ethics Committee approval waiver for the PMS study.</p> <p>After due deliberation, the committee observed that the 5 ethics committees have already approved the study and others are in pipeline. In such circumstances, the committee did not recommend for waiver of Ethics Committee approval in this particular case of cancer immunotherapy.</p> <p>The committee decided that the Ethics committee waiver cannot be given to PMS studies as these are meant for enhancing the data for substantiating efficacy.</p> <p>In view of this, ethics committee waiver granted to RMS for PMS of OSSRON and CHONDRON needs to be reviewed by CDSCO.</p>
Agenda 6	<p><b>Agenda 6</b>  <b>Applicant:</b> M/s Dystrophy Annihilation research Trust, Bangalore  <b>F.No.</b> Stm-CI/06/DART/18-BD</p> <p><b>Presentation:</b> Application for permission to conduct Phase I clinical trial for evaluation of safety of Antisense Oligonucleotide based Multi Exon skipping in a Duchenne Muscular Dystrophy in Patient with Frame Shift Mutation (c7348dupG).</p>	<p>The firm presented the protocol in detail. Even though this was a single patient study proposal, the committee did consider it given its personalized drug design nature for specific mutations and the unmet needs of these patients. After due deliberation, the committee is of opinion that:</p> <ol style="list-style-type: none"> <li>1. Preclinical toxicity data is incomplete w.r.t. hematological, renal and hepatic toxicities with very short follow-up in the animal model for a protocol where the IMP is to be administered for very long durations.</li> <li>2. Rationale for selection of proposed human dose of 5mg/kg once a week based on NOAEL animal dose of 50 mg/kg body weight is not adequately explained / justified without appropriate PK/PD data.</li> </ol> <p>Therefore, the committee recommended that firm should complete further preclinical and PK/PD data along with the appropriate rationale for the proposed dose and submit that data before the committee.</p>

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